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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/626,099	07/26/2000	Li Xing		8236

7590 04/08/2002
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EXAMINER

ALLEN, MARIANNE P

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 04/08/2002

8

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/626,099

Applicant(s)

XING ET AL.

Examiner

Marianne Allen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-3 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: ____.

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DETAILED ACTION

Applicant's arguments with respect to claims 1-3 have been considered but are moot in view of the new ground(s) of rejection.

The rejection of claims 1-3 under 35 USC 101 is withdrawn. Upon further consideration of the claims, the claimed method is considered to be statutory as it is limited to a practical application that produces a concrete, tangible and useful result, namely a pKa value. One of ordinary skill in the art would have known how to use such a value.

The rejection of claims 1-3 under 35 USC 103(a) over Martin et al. is withdrawn in view of applicant's arguments and review of the reference.

Information Disclosure Statement

It is noted that applicant has not filed an information disclosure statement. They are encouraged to do so.

Specification

Applicant is advised that the transmittal papers refer to an appendix of 8 pages containing an SPL software script and that this appendix is referenced in the specification (see page 6, line 17, for example.) However, these pages are not present in the application.

Claim Rejections - 35 USC § 112

Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods as outlined below, does not reasonably provide enablement for determining pKa for all molecules encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

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The claims are directed to determining a pKa for any molecule of interest. Such molecules would include proteinaceous polymers and polynucleotide polymers. Each of these are large and complex molecules with many ionizable sites. The examples are directed to a variety of relatively small organic molecules with relatively few ionizable sites. It is not considered to be so predictable that the method as claimed could be extrapolated to these larger and more complex molecules. Gargallo et al. (*Journal of Computer-Aided Molecular Design*, 13:611-623, 1999) is cited in support of this position. Although the reference predicts pKa using a different computational method, the conclusion is that satisfactory prediction of pKa for homopolynucleotides was limited and could only be achieved when atomic charge was included in the PLS model. (See page 622). It is noted that the claims do not require that the molecules of known pKa in step (a) to be in any way related to the molecule of interest whose pKa is to be predicted. It is further noted that while the specification indicates that five levels produce good results (see page 5), in complex molecules it would appear that many more levels would be required thereby increasing the degree of computational difficulty.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Hurst et al. (U.S. Patent No. 6,208,942) and Hurst et al. (U.S. Patent No. 5,751,605) disclose molecular hologram QSAR, use of partial least squares to predict biological data, and molecular fingerprint bitmaps. (See abstract, claims, and at least columns 2-3 of each patent.) Calculation of pKa does not appear to be disclosed.

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Sivik et al. (U.S. Patent No. 6,093,691) discloses calculating partition coefficients (logp) using commercial software based upon the numbers and types of atoms and their connectivity. (See at least column 23, lines 20-60.) Calculation of pKa does not appear to be disclosed.

Gargallo et al. (*Journal of Computer-Aided Molecular Design*, **13**:611-623, 1999) predicts pKA for nucleic acids using CoMFA data and partial least squares. The structures were built with the Biopolymer module of SYBYL (See abstract; page 612, right column; pages 616-618, Table 3.) Hierarchical atom type connectivity trees do not appear to be disclosed.

Barlow et al. (*Br. J. Pharmac.*, **75**:503-512, 1982) discloses methods for calculating zwitterion constants using experimental data and least-squares fit. Hierarchical atom type connectivity trees do not appear to be disclosed.

It also appears that a commercially available software product would have been available from CompuDrug as part of the Pallas Classic package. The module is called pKalc. (See attached pages from the compudrug.com website.) The pKa value is predicted from the structure. However, the examiner was unable to determine the specific details as to how the computation is performed. It is noted that there were several prior versions of this software that were also commercially available. Applicant is encouraged to provide any information about this product available to them.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen whose telephone number is 703-308-0666. The examiner can normally be reached on Monday-Friday, 7:00 am - 1:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 703-308-4028. The fax phone numbers for

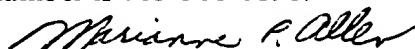
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the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Marianne P. Allen

Primary Examiner

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mpa

April 4, 2002